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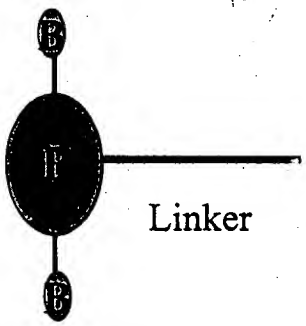
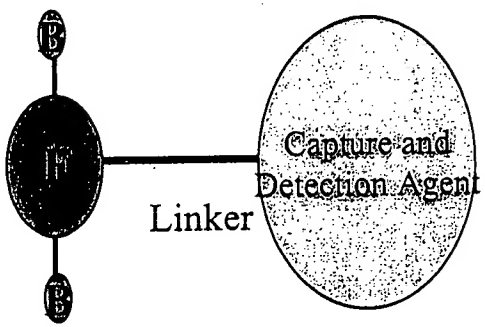
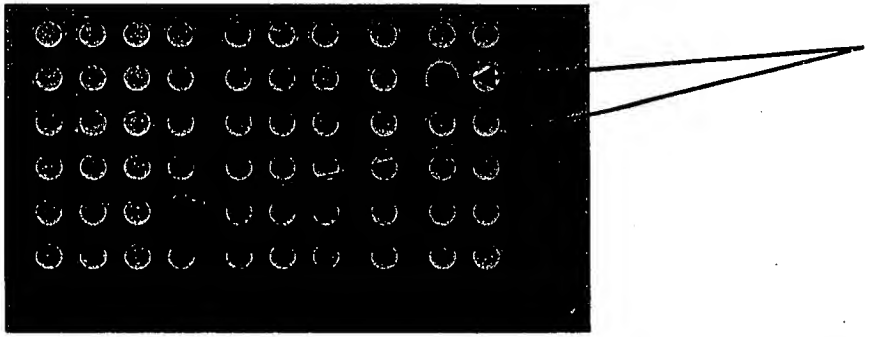
High-throughput Target ID





Library of Bioactive Compounds

Library of Target ID Compounds



Use corresponding activity-based probe to identify the biological target

FIGURE 1

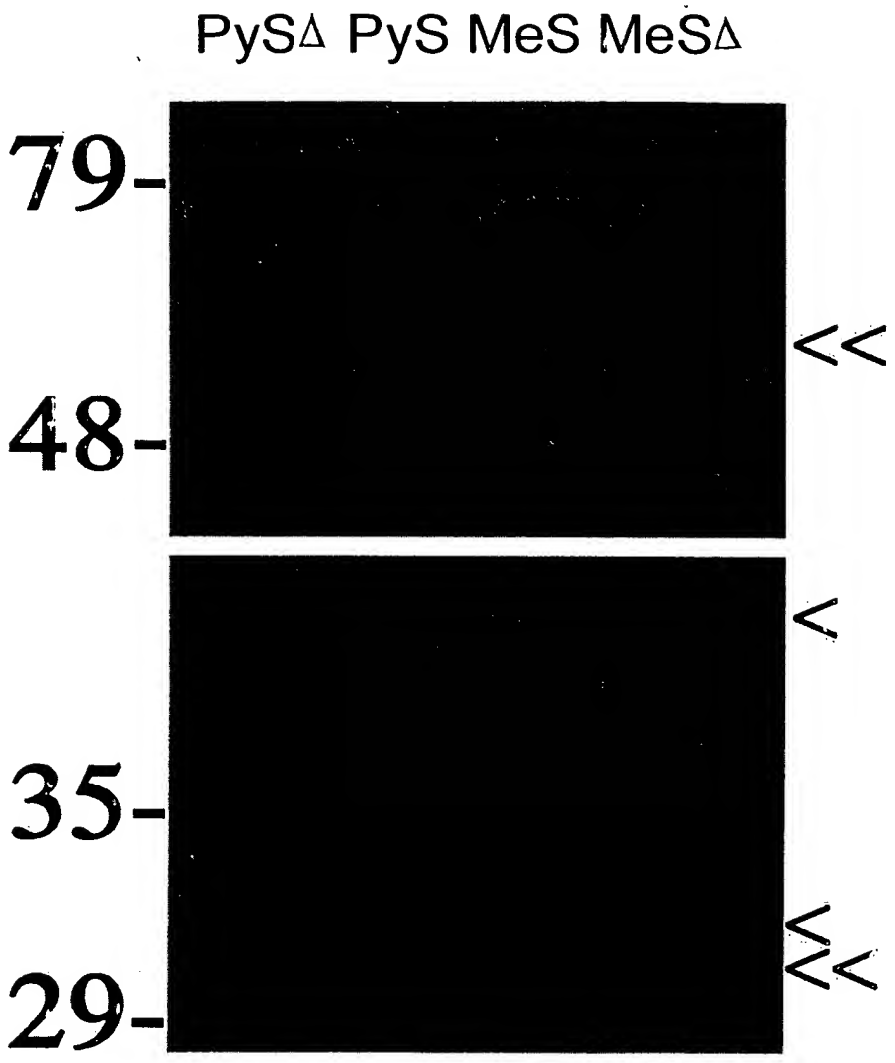
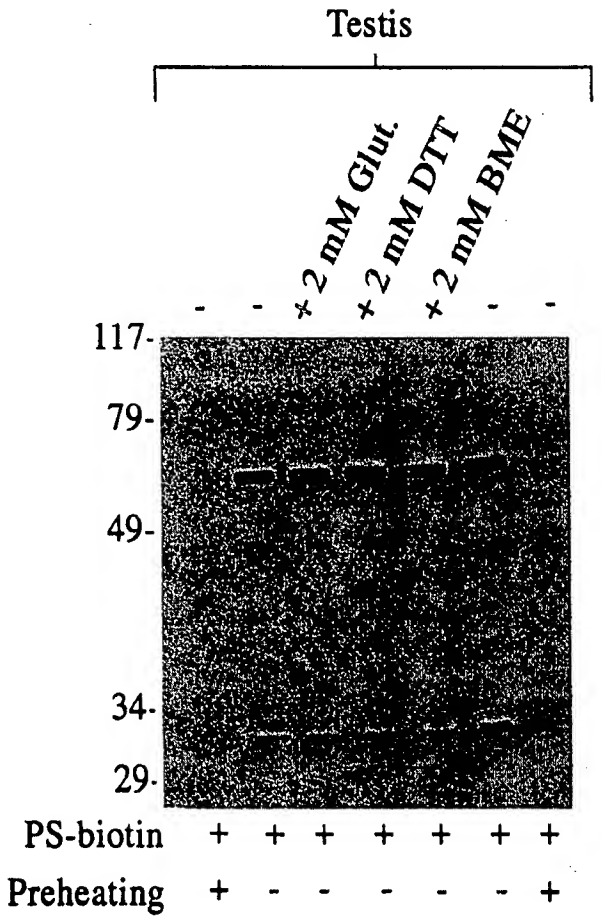


FIGURE 2

TARGET SHT92860



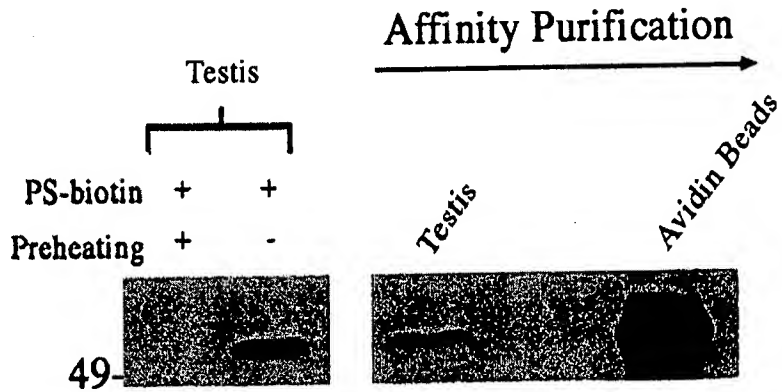
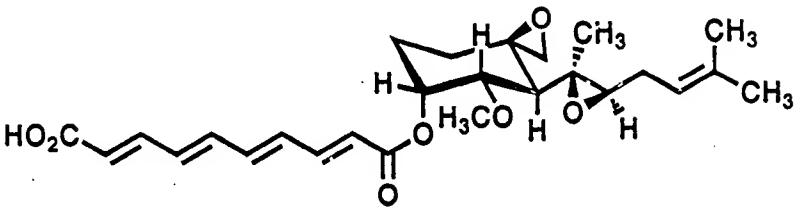
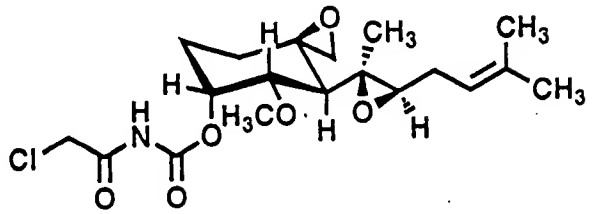


FIGURE 3

TOTEST" SA1998860



Fumagillin



TNP-470

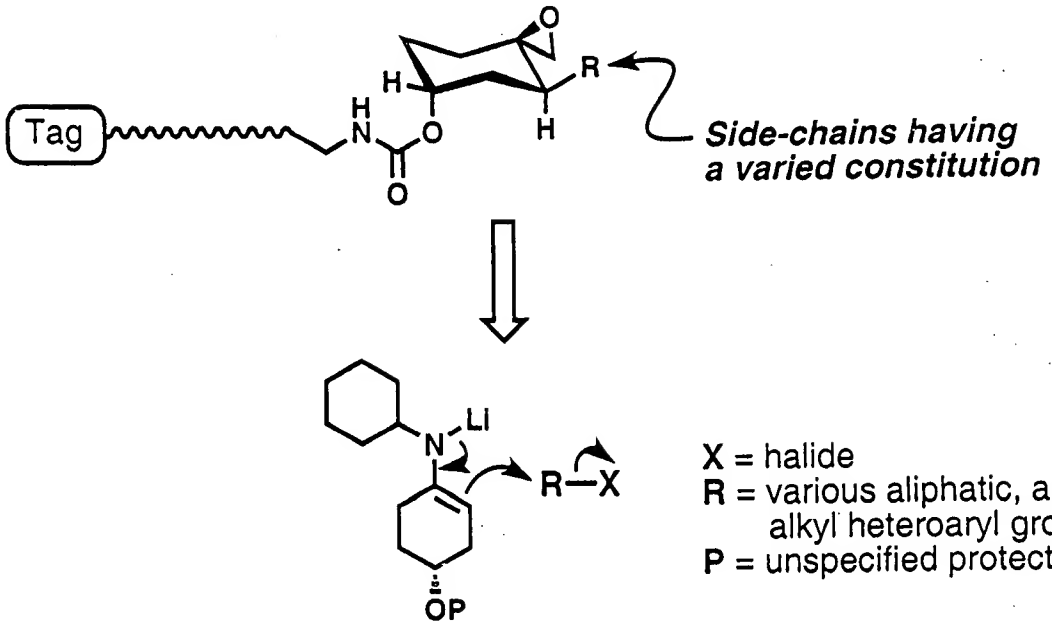


FIGURE 4A

TARGET SHT9660

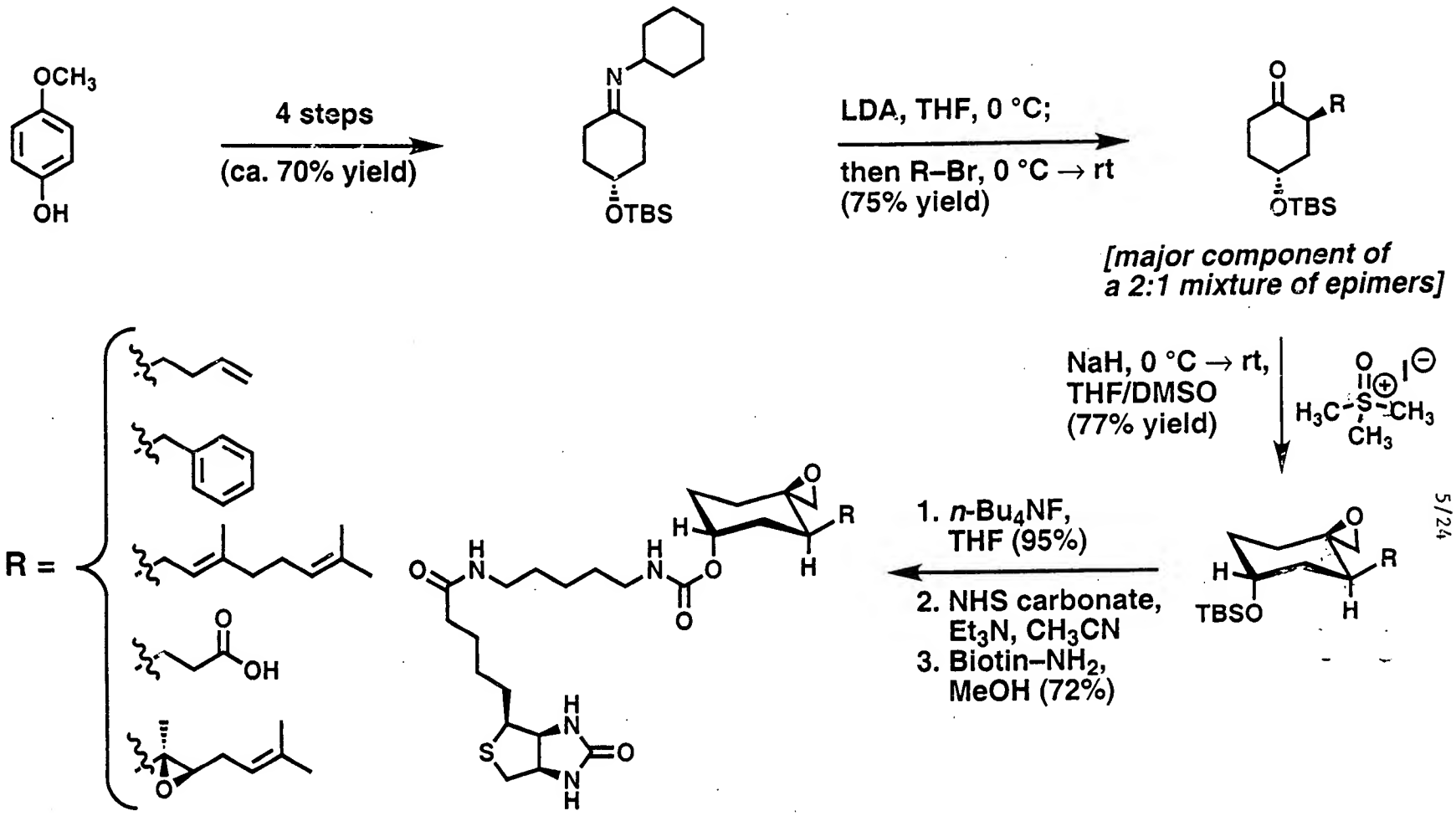


FIGURE 4B

TOTEST SITSEBO

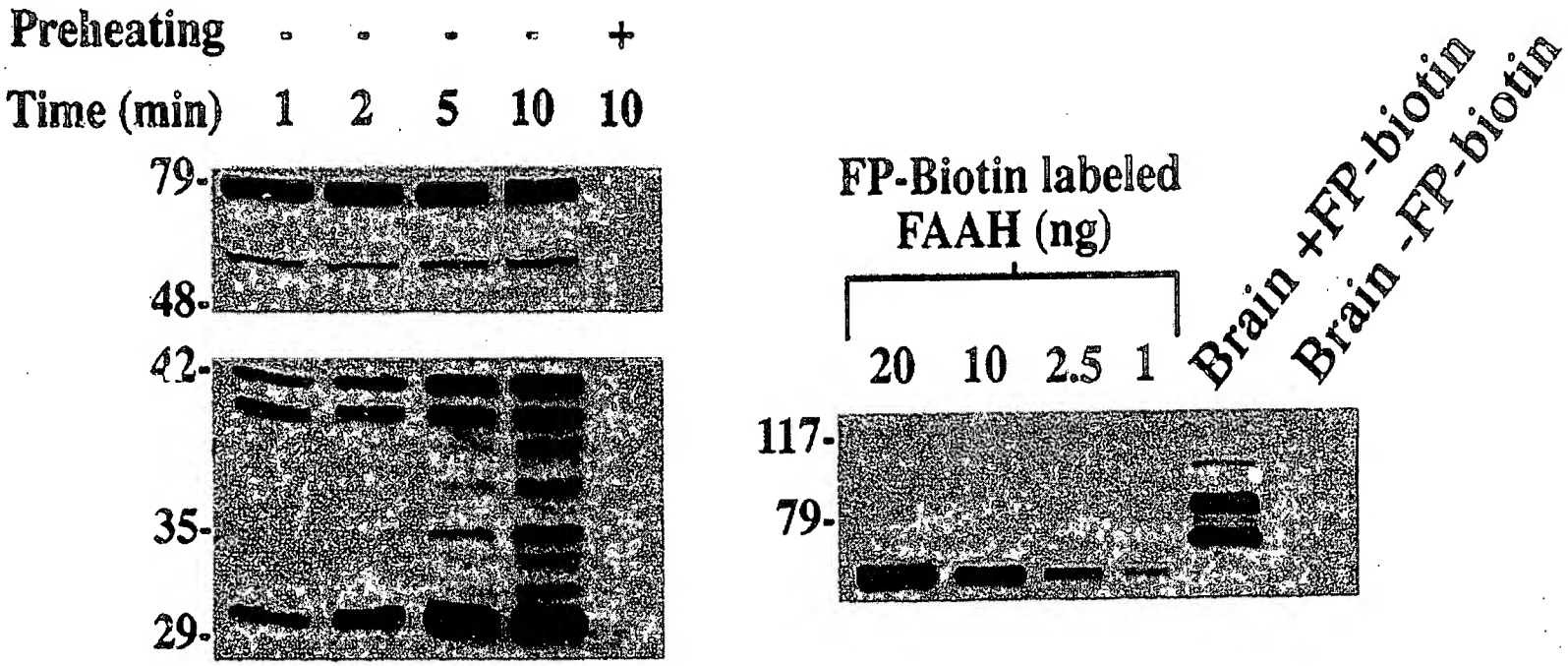
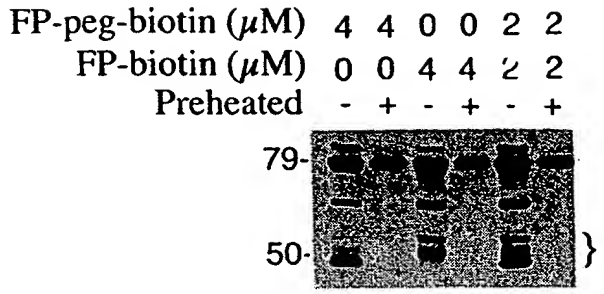


FIGURE 5


FP-peg-biotin (μM) 4 4 0 0 2 2
FP-biotin (μM) 0 0 4 4 2 2
Preheated - + - + - +
79-
50-
}

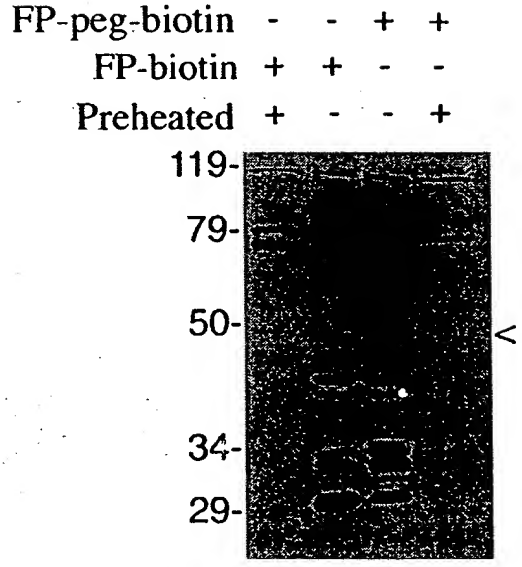

FP-peg-biotin - - + +
FP-biotin + + - -
Preheated + - - +
119-
79-
50-
34-
29-
<

FIGURE 6

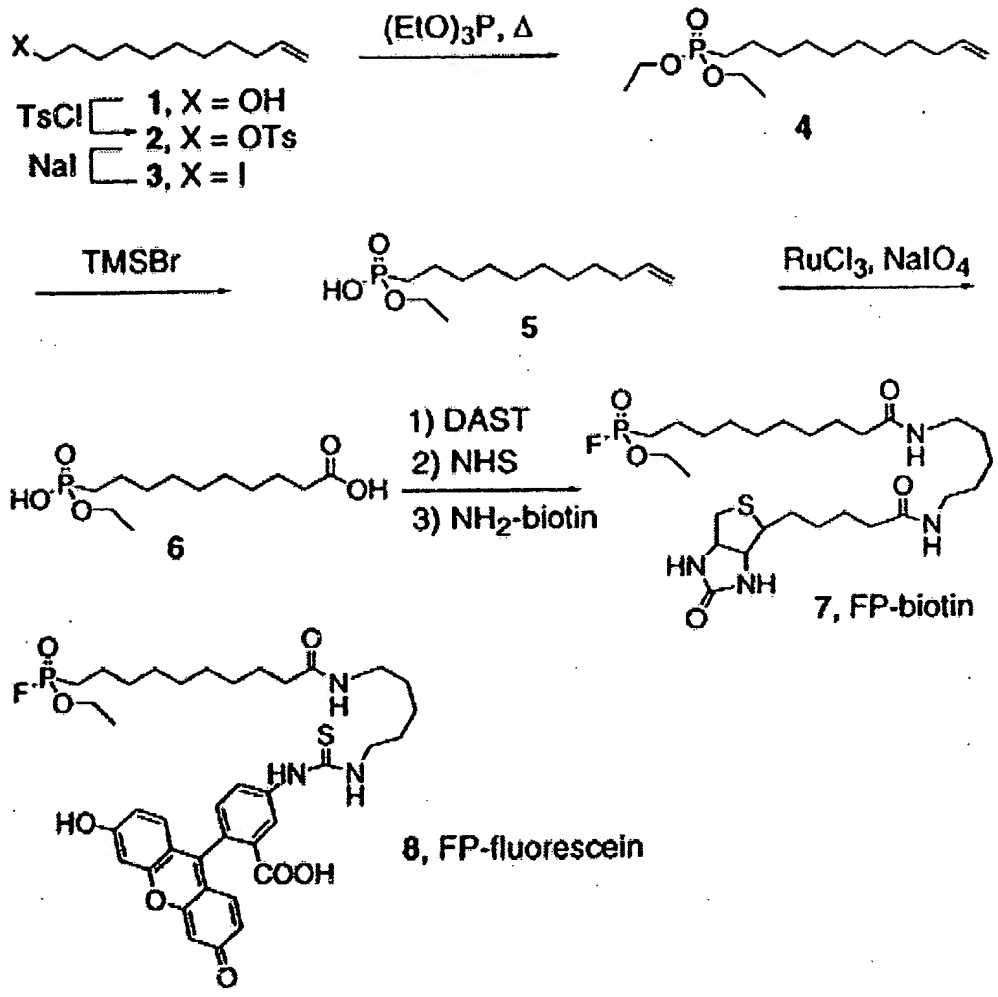

X
(EtO)3P, Δ
TsCl
1, X = OH
2, X = OTs
NaI
3, X = I
4
TMSBr
5
RuCl3, NaIO4
6
1) DAST
2) NHS
3) NH2-biotin
7, FP-biotin
8, FP-fluorescein

FIGURE 8

TOTEST SHEET

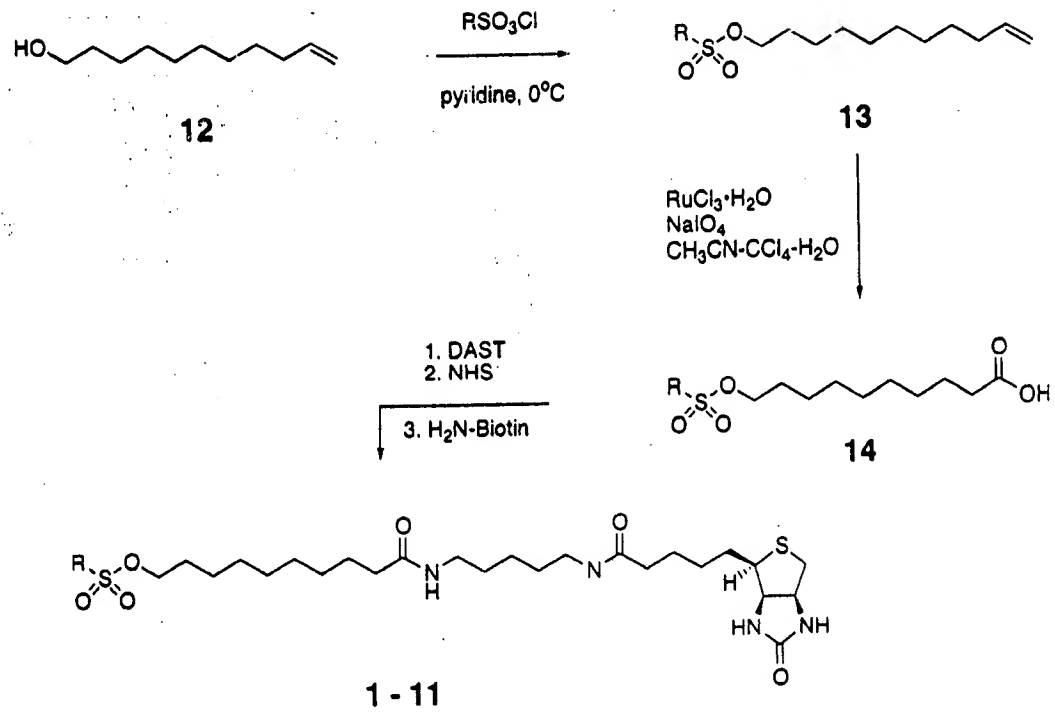
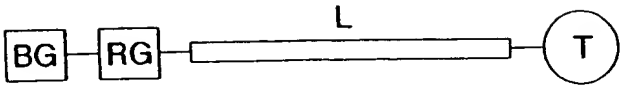


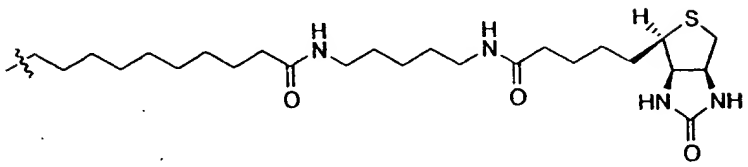
FIGURE 9

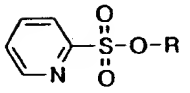
A.

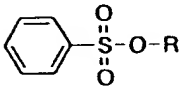


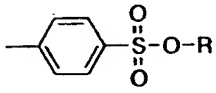
B.

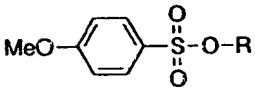
R =

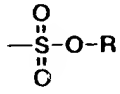


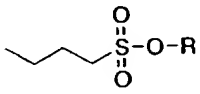
1 

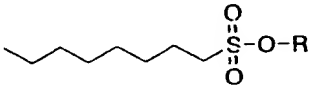
2 

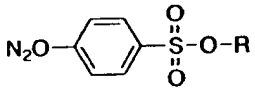
3 

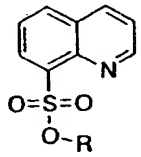
4 

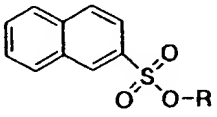
5 

6 

7 

8 

9 

10 

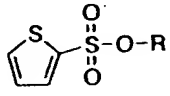
11 

FIGURE 10

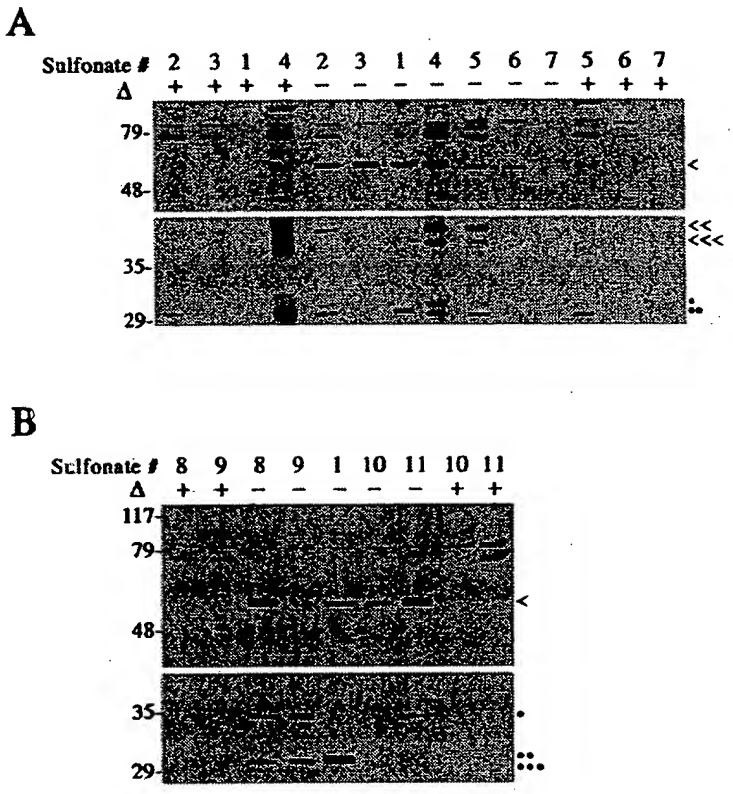

A
Sulfonate # 2 3 1 4 2 3 1 4 5 6 7 5 6 7
Δ + + + + − − − − − − − + + +
79-
48-
35-
29-
B
Sulfonate # 8 9 8 9 1 10 11 10 11
Δ + + − − − − − + +
117-
79-
48-
35-
29-

FIGURE 11

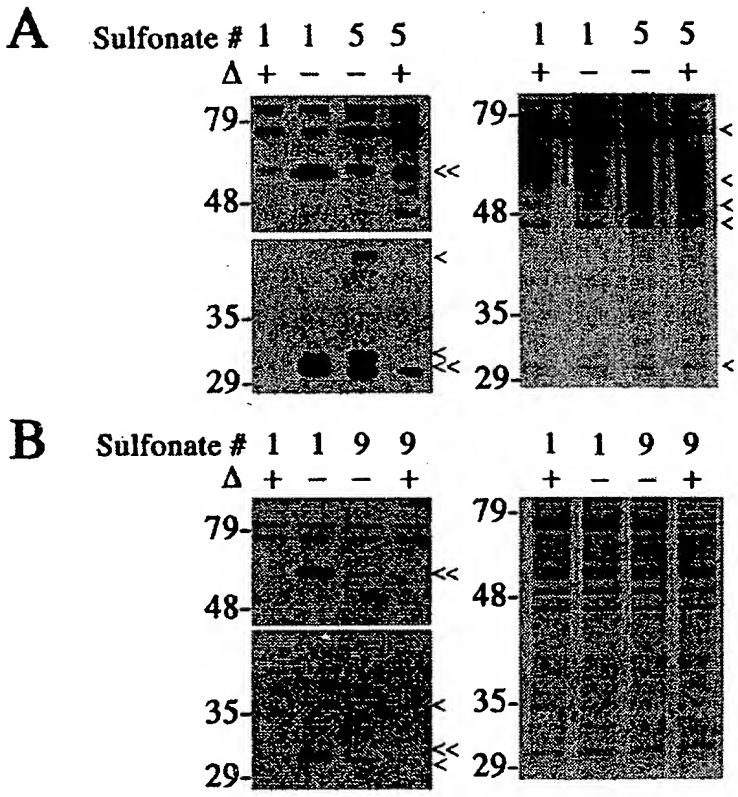
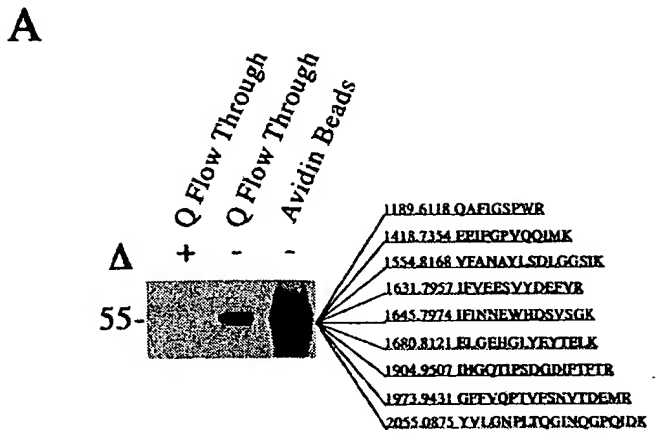
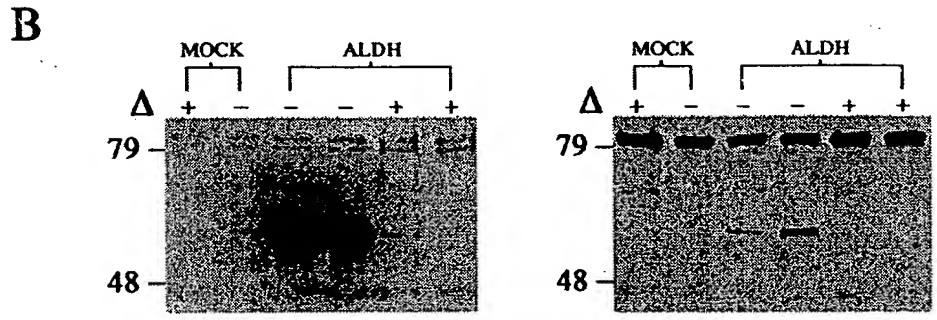
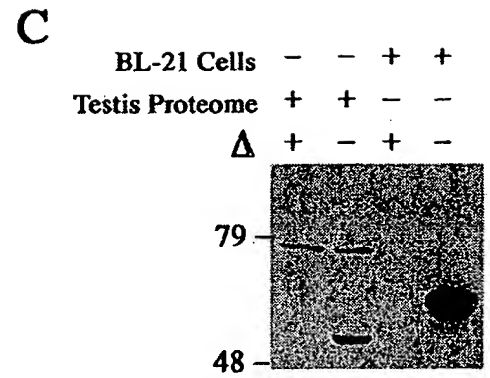

A
Sulfonate # 1 1 5 5
Δ + − − +
79
48
35
29
1 1 5 5
+ − − +
79
48
35
29
B
Sulfonate # 1 1 9 9
Δ + − − +
79
48
35
29
1 1 9 9
+ − − +
79
48
35
29

FIGURE 12


A
Q Flow Through
Q Flow Through
Avidin Beads
Δ + - -
55-
1189.6118 QAFIGSPWR
1418.7354 EEIPGPVQQIMK
1554.8168 YFANAYLSDLGGSIK
1631.7957 IFVEESVYDEFVR
1645.7974 IFINNEWHDSVSGK
1680.8121 ELGEHGLYEYTELK
1904.9507 DHGQTIPSDGDIPTFTR
1973.9431 GPEVQPTVESNYTDEMR
2055.0875 YYLGNPLTQGINQGPQIDK


B
MOCK
ALDH
Δ + - - - + +
79
48
MOCK
ALDH
Δ + - - - + +
79
48


C
BL-21 Cells - - + +
Testis Proteome + + - -
Δ + - + -
79
48

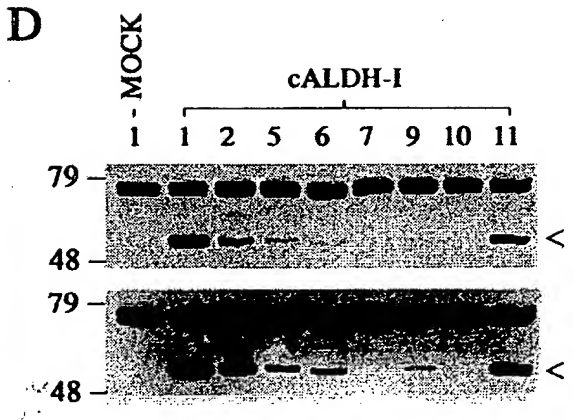
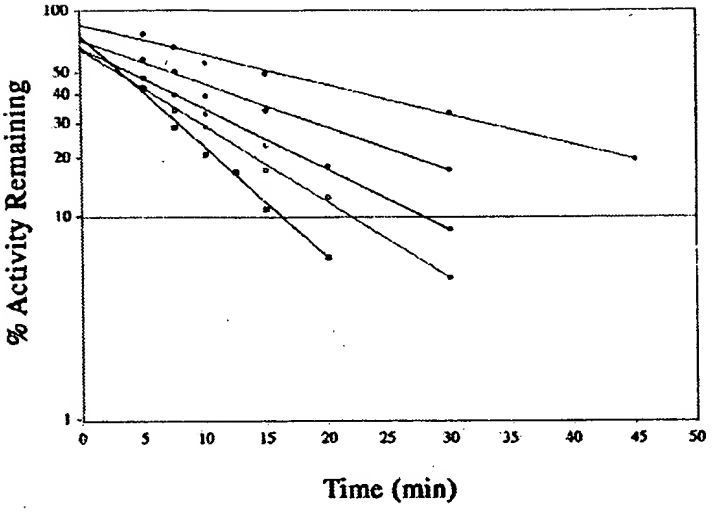

D
- MOCK
cALDH-I
1 1 2 5 6 7 9 10 11
79
48
<
79
48
<

FIGURE 13

PCT/US2004/004000

A



B

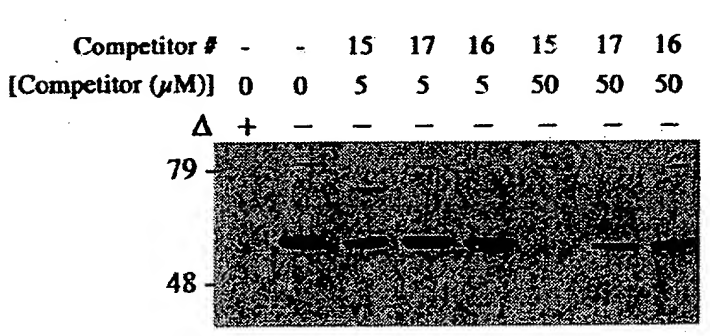


FIGURE 14

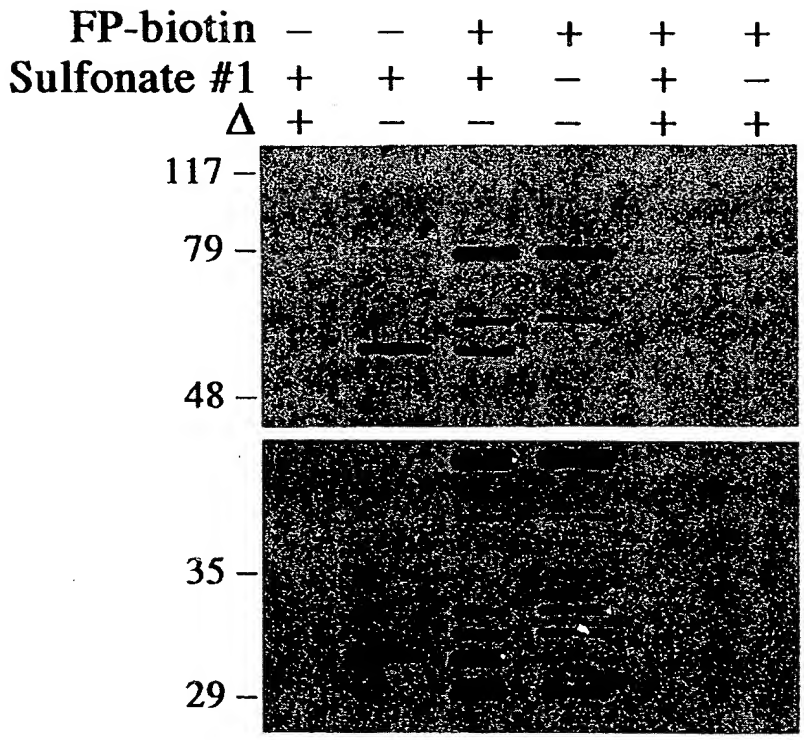


FIGURE 15

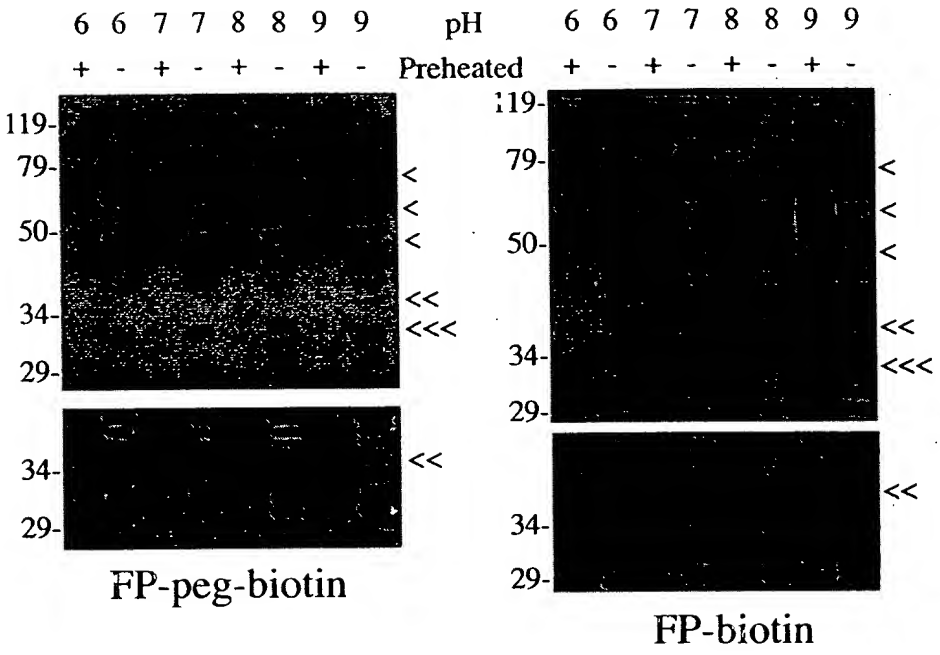

6 6 7 7 8 8 9 9 pH
+ - + - + - + - Preheated
119-
79-
50-
34-
29-
<
<
<
<<
<<<
34-
29-
<<
FP-peg-biotin
6 6 7 7 8 8 9 9
+ - + - + - + -
119-
79-
50-
34-
29-
<
<
<
<<
<<<
34-
29-
<<
FP-biotin

FIGURE 16

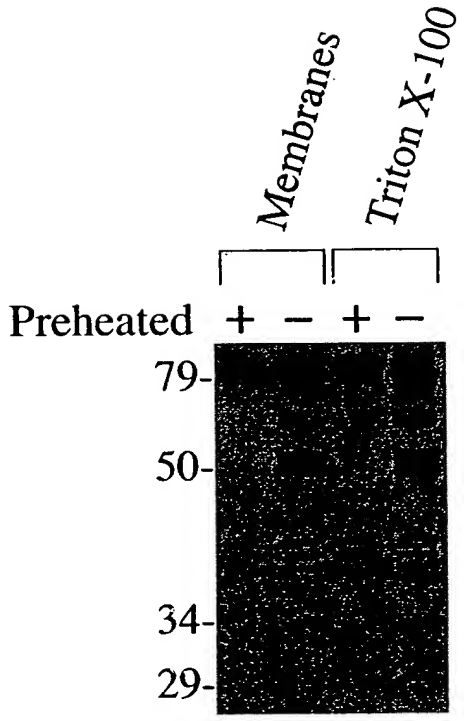


FIGURE 17

WO 94/03594 PCT/US93/07304

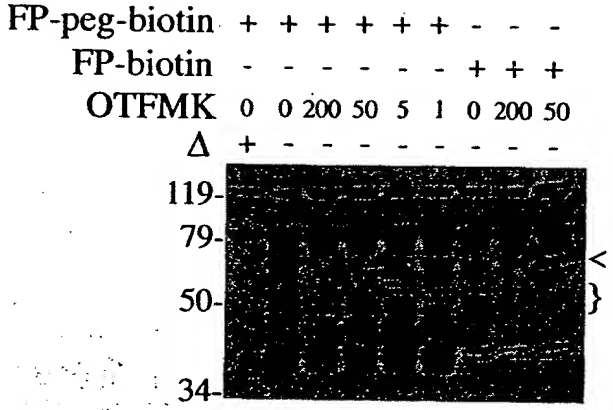


FIGURE 18

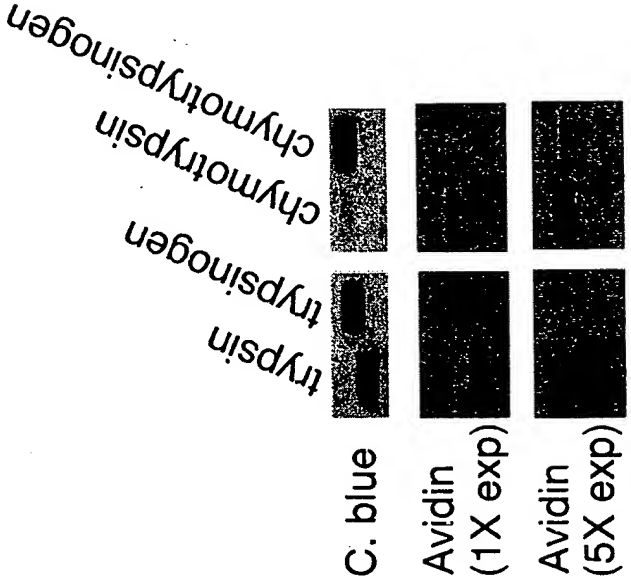


FIGURE 19

PCT/US2004/004504 - 14.04.2004

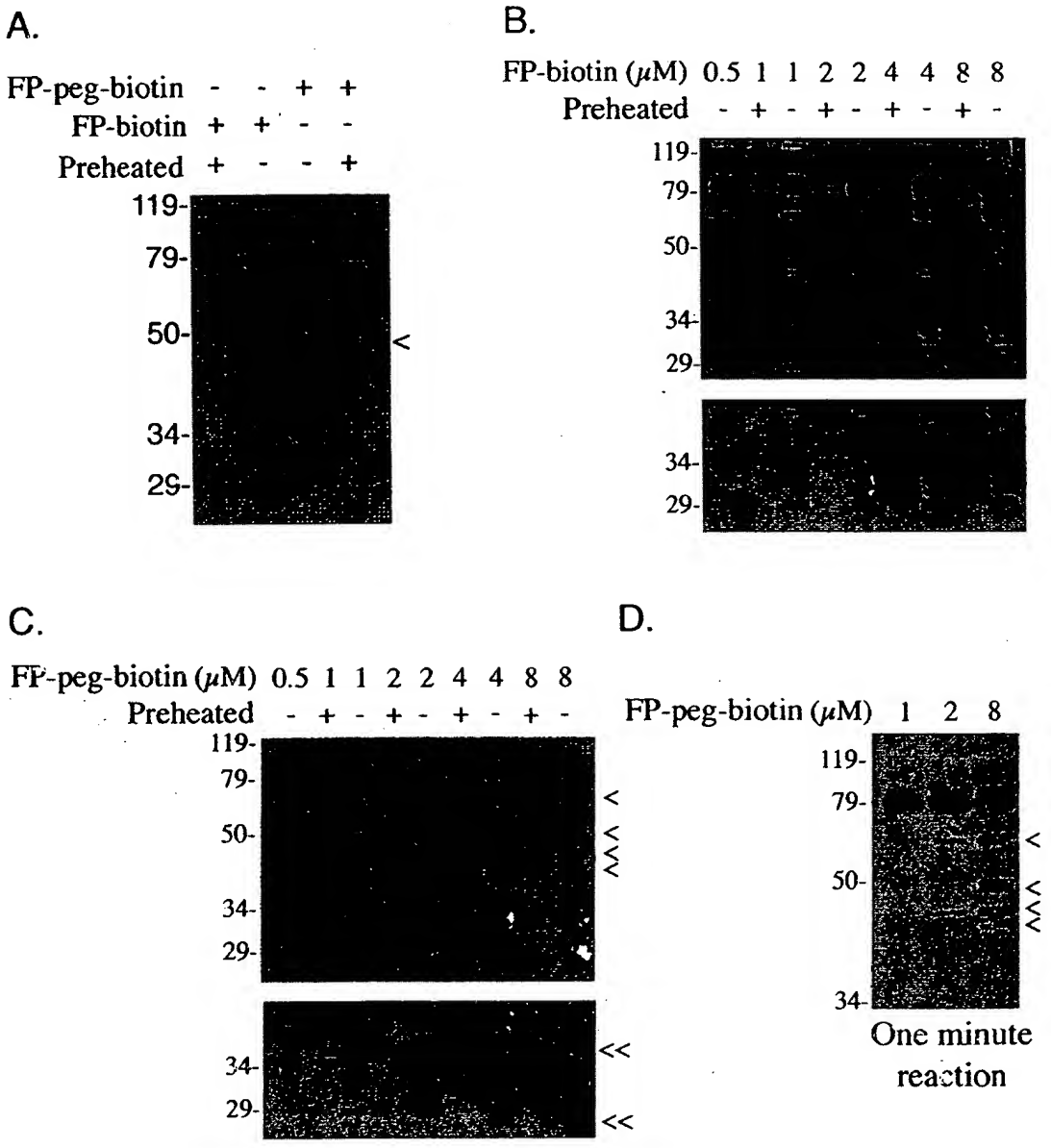

A.
FP-peg-biotin - - + +
FP-biotin + + - -
Preheated + - - +
119-
79-
50-
34-
29-
B.
FP-biotin (μM) 0.5 1 1 2 2 4 4 8 8
Preheated - + - + - + - + -
119-
79-
50-
34-
29-
34-
29-
C.
FP-peg-biotin (μM) 0.5 1 1 2 2 4 4 8 8
Preheated - + - + - + - + -
119-
79-
50-
34-
29-
34-
29-
D.
FP-peg-biotin (μM) 1 2 8
119-
79-
50-
34-
One minute reaction

FIGURE 20

TARGET SHEET

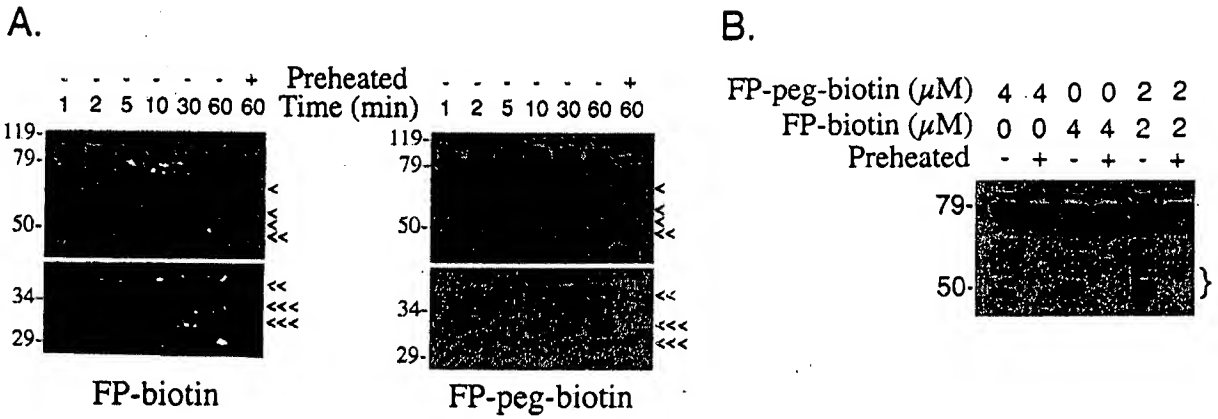


FIGURE 21

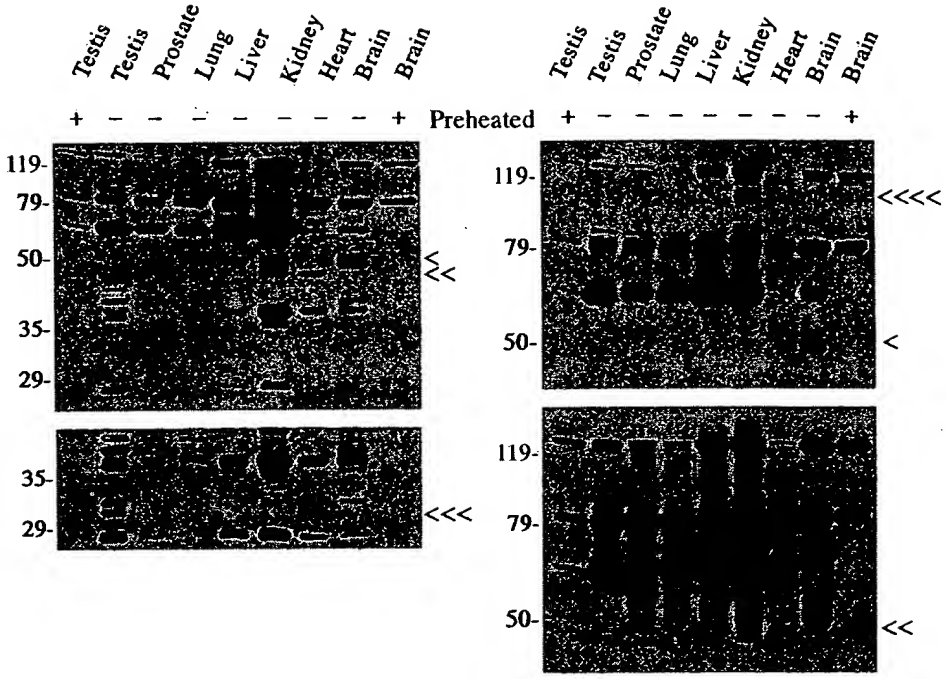
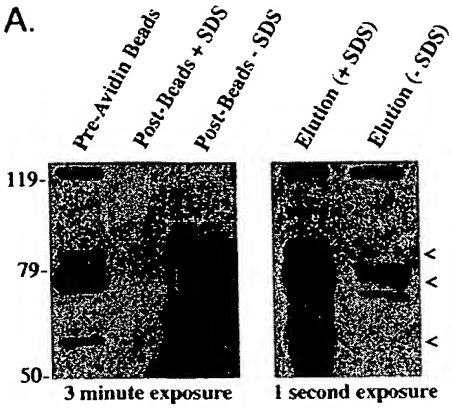

Testis
Testis
Prostate
Lung
Liver
Kidney
Heart
Brain
Brain
+ − − − − − − − +
Preheated
+ − − − − − − − +
119-
79-
50-
35-
29-
<<
<<<
<<<<
<

FIGURE 22


A.
Pre-Avidin Beads
Post-Beads + SDS
Post-Beads - SDS
Elution (+ SDS)
Elution (- SDS)
119-
79-
50-
3 minute exposure
1 second exposure

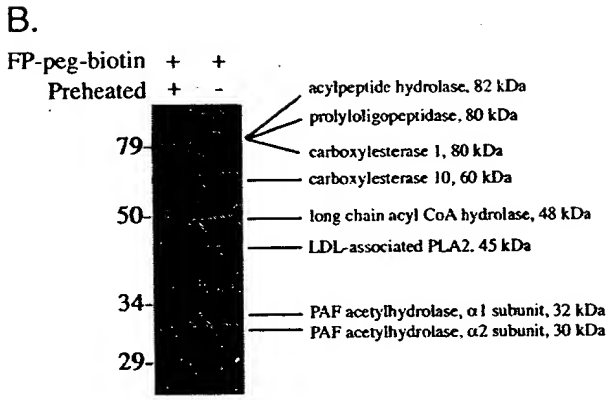

B.
FP-peg-biotin + +
Preheated + -
79-
50-
34-
29-
acylpeptide hydrolase, 82 kDa
prolyloligopeptidase, 80 kDa
carboxylesterase 1, 80 kDa
carboxylesterase 10, 60 kDa
long chain acyl CoA hydrolase, 48 kDa
LDL-associated PLA2. 45 kDa
PAF acetylhydrolase, α1 subunit, 32 kDa
PAF acetylhydrolase, α2 subunit, 30 kDa

FIGURE 23